

| Section A. | Project Information | | | | |
|-------------------------|---|-------------------------------|-----------------------|-----------------------|----------------|
| Project Title | TSRI Center for hESC Researc | :h | | | |
| | Limited to 300 Characters | | | | |
| | | | | | |
| Project Start D | Date Jul 1, 2007 | Construction Start Date | Jul 2, 2007 | Occupancy Date | Sep 1, 2007 |
| | | | | | |
| Total Part Two | Funds Requested for Shared | Laboratory Space | \$ 945,583 | | |
| Total Part Two | Funds Requested for Stem C | ell Techniques Course | | | |
| Total Capital F | Funds Requested | | \$ 1,650 | | |
| Note: All green f | fields are calculated values. Do no | ot enter a value in the field | I. | | |
| | te whether you propose to a pace, or just the Shared Lab | | Stem Cell Technique | es Course along with | the Shared |
| Share | d Research Laboratory only | ○ Sha | red Research Laborato | ory and Stem Cell Tec | hniques Course |
| | | | | | |

NOTE: Please be aware that any information you provide in this form will be made publically available.

| Section A. 1. Program Director | | | | | | | |
|---|-----------|-------|----------------------------------|--|--|--|----------------------|
| Name | Professor | Peter | | G | Schultz | | |
| | Prefix | First | | Middle | Last | | Suffix |
| Email (office) schultz@scripps.edu This email address identifies you to CIRM. Please use this email address for correspondence with CIRM. | | | | ress for all | | | |
| Application Number CL1-00502-1 | | | This field sho received via e | uld fill automatically, b email from CIRM, in the | pased on the email addr form "XX9-99999-9", v | ess. If not, enter the numbe where "X" is a letter, and "9" | r you is a digit. |

| Section A. 2. Facilities Contact | | | | | | | | | |
|------------------------------------|--------|----------|-------------------------|--|--------------|----------------------------|----------------|---|--------|
| Name | Mr. | | Benjamin | F | | Morris | | | |
| | Prefix | | First | Mi | iddle | Last | | | Suffix |
| Institutio | on | Scripp | s Research Institute | | | | | | |
| Other Institution | | | | | | | | our institution is not listed ntify the name of the instit | • |
| Position Title | | V.P., Fa | acilities Services | | | | • | | |
| Department | | Faciliti | es Services | | | | | | |
| Address | | 10550 | North Torrey Pines Road | | | | | | |
| | | TPC-16 | 5 | | | | | | |
| | | | | | | | | | |
| City | | La Joll | a | | | | CA | Zip Code 92037 | |
| Phone N | lumber | (858) 7 | 784-8088 | Ext | | Fax Number | (858) 784-8118 | | |
| Email (office) bmorris@scripps.edu | | • | This email correspon | address identifies dence with CIRM. | you to CIRM. | Please use this email addı | ess for all | | |



Section A. 3. Public Abstract

See Appendix A.

Section A. 4. Statement of Benefit to California

See Appendix A.



| Section B. Labo | ratory Renovation Plan | |
|---------------------|----------------------------------|-------------------------|
| Project Manager | James Jaeger | Construction Supervisor |
| Title | Facilities Coordinator | Title |
| Company/Institution | n The Scripps Research Institute | Company/Institution |

Describe plans for development/renovation of the shared laboratory space including fixed equipment costs. Include a description of the current space and how it will be renovated and reconfigured to form the laboratory. Include as attachments one 11x17 page of the current floor plan space and one 11x17 page of proposed floor plan of the renovated space. Describe all renovations that will be done. Describe how the project will be managed and tracked, as well as how change orders will be handled. For laboratories that are proposed to be located in leased space, provide information regarding the institution's long-term access to the leased space. Describe plans and schedule for all phases of development including design, construction, and installation of equipment leading to a functional laboratory. Give a proposed contingency plan in case of cost overruns. Any additional costs due to budget overruns will be the responsibility of the grant recipient. (narrative limited to 3 pages)

The proposed space, Lab 3020 in the 3030 Science Park Building, is a total of 1,560 square feet and is divided into 3 areas:

- 1. wetlab space with (2) island benches 882 s.f.
- 2. cell culture room 217 s.f.
- 3. (3) offices 461 s.f.

This renovated space has been provided by TSRI and can be used for nonapproved human embryonic stem cells. Renovations of the laboratory will consist solely of modifications to the power at the equipment wall. The scope of work is as follows:

- Conversion of (2) 120v, 20a receptacles to (2) 208v, 20a receptacles

Other than the above mentioned modifications, the space is already configured for the needs of the proposed user and work processes.

The construction will be managed and tracked by the TSRI Department of Facilities Planning and Construction. They will meet with the contractor and Professor Schultz to coordinate all parties involved. Change orders, if necessary, will be issued to the contractor and will be paid for by the 10% construction contingency set aside for such changes.

With such a minimal scope, design will be completed in (2) business days; construction will be take approximately (2) days as well. Installation of equipment is expected to last for a duration of (1) day.

The 3030 Science Park Building is leased by TSRI from REIT management for a duration of 12 more years. TSRI will have complete access to the space for that entire duration.

The Schultz lab will be directly responsible for cost overruns due to user introduced change orders. TSRI will be directly responsible for cost overruns due to unforeseen conditions or building deficiencies.



Section B. 1. Schedule/Timeline and Drawdown of Funds Table

Provide a realistic schedule and drawdown of funds for completing each activity/milestone, as indicated below.

| # | Activity/Milestone | Start Date | Completion or Milestone Date | Amount of CIRM funds to be drawn |
|----|--|------------|---------------------------------|----------------------------------|
| 1 | Grant Award (estimate) | | Jul 1, 2007 | |
| 2 | Request for Planning Funds (10% of Construction Costs) | | July 2, 2007 | \$ 165 |
| 3 | Prepare Preliminary Plans | | July 9, 2007 | |
| 4 | Approval of PPs | | July 16, 2007 | |
| 5 | Prepare Working Drawings | | July 18, 2007 | |
| 6 | Approval of WDs | | July 25, 2007 | |
| 7 | Request Construction Contract funds (80% of Construction Costs) | | August 1, 2007 | \$ 1,320 |
| 8 | Advertise for Construction Contract | | August 8, 2007 | |
| 9 | Award Construction Contract | | August 15, 2007 | |
| 10 | Construction Activities | | August 18, 2007 | |
| 11 | Completion of Equipment Purchases | | ? | |
| 12 | Request Equipment Purchase funds | | ? | \$943,933 |
| 13 | Beneficial Occupancy | | September 1, 2007 | |
| 14 | Notice of Completion | | September 8, 2007 | |
| 15 | Request Construction Completion Amount (10% of Construction Funding) | | September 15, 2007 | \$ 165 |

[&]quot;Preliminary Plans" (PPs) represent approximately 35 percent of the design effort, or may be considered the product of completing the "Design Development" (DDs) phase of architectural work.

[&]quot;Working Drawings" (WDs) represent drawings and specifications from which a contractor may determine the full extent of work contemplated in the project for purposes of submitting a bid; may be referred to as completion of "Construction Documents" (CDs) phase of architectural work.



Section B. 2. Budget

Provide a complete budget for the renovation that includes construction costs, design fees, administration of the project, other costs (i.e. installation of equipment) and a construction contingency (limited to 7-10% of the construction budget). Identify the amount of CIRM funds requested and the matching funds (construction requires 20% matching funds). Provide a complete budget for movable equipment (equipment requires 20% matching funds). (narrative limited to 3 pages)

(Note: An Excel spreadsheet can be attached as long as the total submission for this Section is limited to 3 pages)

| Major Equipment: The equipment listed below (1.10) are your basis requirements for a cell sulture facility and expected to |
|--|
| I. Major Equipment: The equipment listed below (1-10) are very basic requirements for a cell culture facility and expected to |
| have over five years useful life. More specifically: |
| |
| 1. Centrifuge (bench top)(Thermo Fisher)\$ 7,449.00 |
| Centrifuge Rotor\$ 2,153.00 |
| Rotor Adaptors\$ 600.00 |
| · |
| Total\$10,202.00 |
| Rationale: For centrifuging cells or viral particles in tube and plate format |
| |
| 2. Milli-Q Water System (Fisher)\$ 8,004.00 |
| Rationale: For purified water used in various research applications |
| Rationale: For purified water used in various research applications |
| |
| 3. iCycler with 96-well module (BioRad) |
| Rationale: For conducting PCR to analyze gene expression of hESCs |
| nationale. For confidenting Ferror analyze gene expression of neses |
| 1 |
| 4. Freezers |
| 2 -80 Freezers (Thermo Fisher) (\$14,297.00 ea)\$ 28,594.00 |
| 2 -20 Freezers (Thermo Fisher) (\$5,970.00 ea)\$ 11,940.00 |
| 2 4 Freezers (Thermo Fisher) (\$5,343.00 ea)\$ 10,686.00 |
| |
| Total\$ 51,220.00 |
| Rationale: For reagent storage |
| |
| 5. Liquid Nitrogen Freezer (Thermo Fisher)\$ 18,663.00 |
| |
| Rationale: For cell storage |
| |
| 6. Multidrop Microplate Dispenser (Thermo Fisher)\$ 6,844.00 |
| Rationale: For dispensing cells and media for screens |
| nationale. For dispensing cens and media for serectis |
| |
| 7. Gel Doc System (BioRad)\$12,822.00 |
| PC for Gel Doc\$ 2,625.00 |
| Total\$ 15,447.00 |
| |
| Rationale: For visualizing/quantifying DNA, RNA and protein samples in molecular biology |
| |
| 8. Plate Washer (Thermo Fisher)\$11,350.00 |
| Vacuum System\$ 915.00 |
| Total\$ 12,265.00 |
| , , |
| Rationale: For conducting immunostaining for high content screening |
| |
| 9. Gene Pulser (BioRad)\$ 6,348.00 |
| Rationale: For electroporating DNA and RNA into cells |
| nationale. For electroporating DNA and NNA into cells |
| |
| 10. 4 Incubators (Thermo Fisher)(\$6,626.00 ea)\$ 26,504.00 |
| |
| |
| la time and the contract of th |
| In addition, we request funds for a versatile imaging system for high throughput screens: |
| 1. Evotec Opera\$712,569.00 |
| Rationale: Stem cell differentiation results in complex changes of multiple phenotypes including cell number, cell cycle |
| distribution, marker expression, cell-cell interactions, and cell morphology. We have found that the most versatile method for |
| |
| screening small molecules and genomics for modulators of differentiation is high content imaging which allows for detailed |



Section B. 2. Budget (continued)

monitoring of cellular states. An excellent commercial system for these experiments is the Evotec Opera, a high throughput spinning disk confocal microscope that allows imaging of four colors and is fully compatible with automation. We have used this system extensively for our own studies of murine ESCs, but the system is at GNF, is only available on nights and weekends, and is not available for studies with hESCs.

| Major Equipment Subtotal | \$876,040.00 | |
|------------------------------|--------------|--------------|
| California Sales Tax (7.75%) | \$ 67,893.00 | |
| | | |
| Major Equipment Grand Total | | ¢0/13/033/00 |



Section B. 3. Budget Summary Table

Complete the budget summary for the use of CIRM funds.

Note: All colored fields contain calculated data. Please do not enter anything in those fields.

| Other Project Costs | | | | | | | |
|--|------|--------------|------------------|---------------------|--|--|--|
| Budget Category | | Total Budget | CIRM Grant Funds | Institutional Match | | | |
| Construction Contract Costs | | \$ 1,500 | \$ 1,500 | \$ 000 | | | |
| Other Construction Costs (institutional) | | \$ 000 | \$ 000 | \$ 000 | | | |
| Subtotal Construction | | \$ 1,500 | \$ 1,500 | \$ 000 | | | |
| Design Fees | | \$ 000 | \$ 000 | \$ 000 | | | |
| Administrative Costs | | \$ 000 | \$ 000 | \$ 000 | | | |
| Construction Contingency | | \$ 150 | \$ 150 | \$ 000 | | | |
| Total Construction | | \$ 1,650 | \$ 1,650 | \$ 000 | | | |
| Movable Equipment | | \$ 943,933 | \$ 943,933 | \$ 000 | | | |
| Total Budget | | \$ 945,583 | \$ 945,583 | \$ 000 | | | |
| | | | | | | | |
| Gross Square Feet | 1680 | \$ 0.98 | \$ 0.98 | Const Costs/GSF | | | |
| Assignable Square Feet | 1560 | \$ 1.06 | \$ 1.06 | Const Costs/ASF | | | |



Section B. 4. Institutional Commitment

Provide a detailed description of the amount and source of matching funding for each request that requires matching funds. The requirement of matching funds can be satisfied if the institution can document funds, excluding other grant funds, committed to similar projects (i.e., renovation of lab space and equipment purchase) after January 1, 2005. Detail the use of the space after the three year period is completed. (narrative limited to 2 pages)

TSRI recently completed the renovation of the proposed lab space (Lab 3020) at a cost of approximately \$421,621.20. The breakdown is as follows:

Cost of 3030 Science Park T.I. = \$20,000,000.00 3030 Science Park Square Footage = 74,000 Cost per square foot = \$270.27 Square Footage of Proposed Space (Lab 3020) = 1,560 Cost to Build Existing Space (Lab 3020) = \$421,621.20

The cost of \$421,621.20 to renovate the lab space therefore satisfies TSRI's obligation of a 20% funding match.

After the three year CIRM funding period, the facility will continue to function as a human embryonic stem cell facility assuming funds are available for its operation (we will begin to identify funds in year 2-3 of the grant).



Section C. Stem Cell Techniques Course (if applicable) Based on the information provided in Part One of the application describing the course, include a justification of the additional space required and additional equipment requested, if any. Include additional square footage and provide as an attachment one 11x17 page of the proposed floor plan of the renovated space. (narrative limited to 1 page)



Section C. 1. Schedule and Drawdown of Funds Table (if applicable)

Provide a realistic schedule and drawdown of funds for completing each activity/milestone, as indicated below.

| # | Activity/Milestone | Start Date | Completion or Milestone Date | Amount of CIRM funds to be drawn |
|----|--|------------|------------------------------|----------------------------------|
| 1 | Grant Award (estimate) | | | |
| 2 | Request for Planning Funds (10% of Construction Costs) | _ | | \$ 000 |
| 3 | Prepare Preliminary Plans | | | |
| 4 | Approval of PPs | | | |
| 5 | Prepare Working Drawings | | | |
| 6 | Approval of WDs | | | |
| 7 | Request Construction Contract funds (80% of Construction Costs) | _ | | \$ 000 |
| 8 | Advertise for Construction Contract | | | |
| 9 | Award Construction Contract | | | |
| 10 | Construction Activities | | | |
| 11 | Completion of Additional Equipment Purchases | | | |
| 12 | Request Additional Equipment Purchase funds | | | |
| 13 | Beneficial Occupancy | | | |
| 14 | Notice of Completion | | | |
| 15 | Request Construction Completion Amount (10% of Construction Funding) | | | \$ 000 |

[&]quot;Preliminary Plans" (PPs) represent approximately 35 percent of the design effort, or may be considered the product of completing the "Design Development" (DDs) phase of architectural work.

[&]quot;Working Drawings" (WDs) represent drawings and specifications from whicha contractor may determine the full extent of work contemplated in the project for purposes of submitting a bid; may be referred to as completion of "Construction Documents" (CDs) phase of architectural work.

[&]quot;Additional Equipment" represents equipment to be used for the Stem Cell Techniques Course.



Section C. 2. Budget (if applicable)

| Provide a complete budget for the additional renovation that includes construction costs, design fees, administration of the project, other costs (i.e. installation of equipment) and a construction contingency (limited to 7-10% of the construction budget). Identify the amount of CIRM funds requested and the matching funds (construction requires 20% matching funds). Provide a | | | | | |
|---|--|--|--|--|--|
| complete budget for additional movable equipment (equipment requires 20% matching funds). (narrative limited to 3 pages) (Note: An Excel spreadsheet can be attached as long as the total submission for this Section is limited to 3 pages) | | | | | |
| (Note: All Exect spreadsheet can be attached as long as the total sabilission to this section is infliced to 5 pages) | | | | | |
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Section C. 3. Budget Summary Table (if applicable)

Complete the budget summary for the use of CIRM funds.

Note: All colored fields contain calculated data. Please do not enter anything in those fields.

| Other Project Costs | | | | | | |
|--|--------------|------------------|---------------------|--|--|--|
| Budget Category | Total Budget | CIRM Grant Funds | Institutional Match | | | |
| Construction Contract Costs | | | | | | |
| Other Construction Costs (institutional) | | | | | | |
| Subtotal Construction | | | | | | |
| Design Fees | | | | | | |
| Administrative Costs | | | | | | |
| Construction Contingency | | | | | | |
| Total Construction | | | | | | |
| Additional Movable Equipment | | | | | | |
| Total Budget | | | | | | |
| | | | | | | |
| Gross Square Feet | \$ 0.00 | \$ 0.00 | Const Costs/GSF | | | |
| Assignable Square Feet | \$ 0.00 | \$ 0.00 | Const Costs/ASF | | | |



Section D. Signature Page

Complete, save, and print Part Two of the Shared Research Laboratory Grant Information.

Submit electronic application as an email attachment to laboratory@cirm.ca.gov no later than 5:00pm PST on March 16, 2007.

Mail* the original executed Part Two application and five (5) copies to:

Shared Research Laboratory Grant Application

California Institute for Regenerative Medicine 210 King Street San Francisco, CA 94107

*Mailing must be postmarked no later than March 16, 2007. Applications will not be accepted after these deadlines.

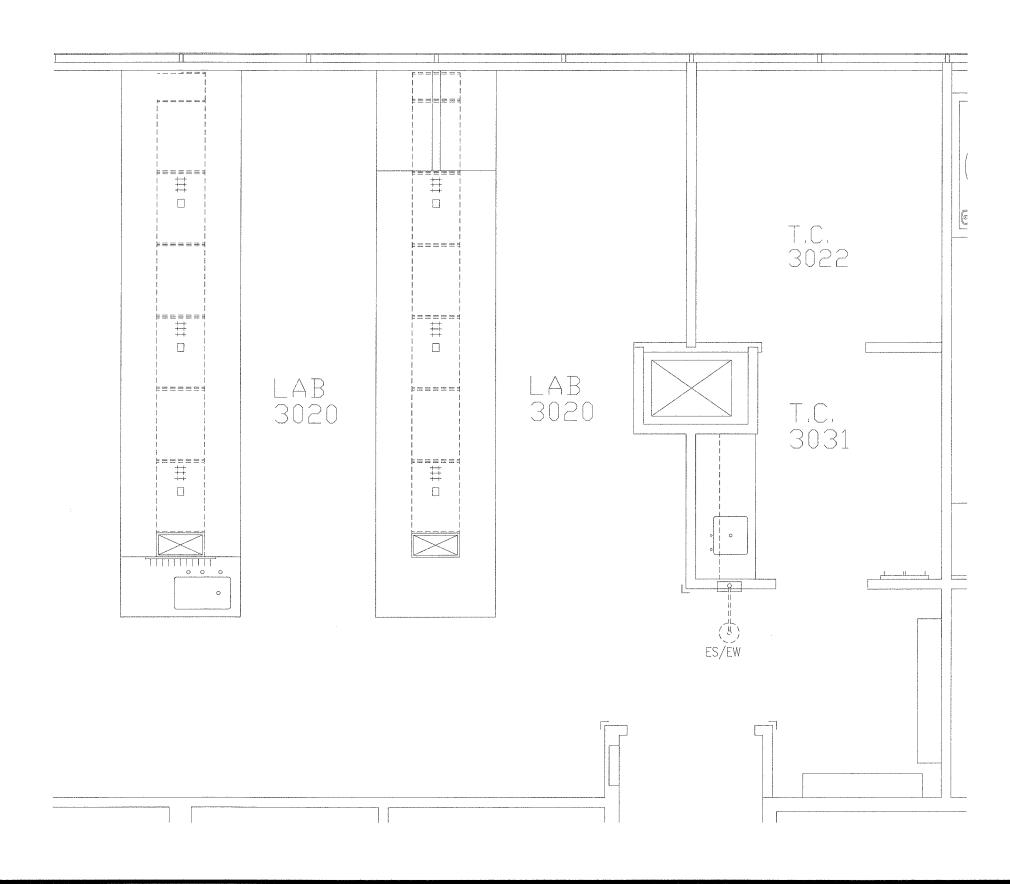
| Project Start Date Jul 1, 2007 Construction Start Date Jul 2, 2007 Occupancy Date Sep 1, 2007 Total Part Two Funds Requested for Shared Laboratory Space \$ 945,583 Total Part Two Funds Requested for Stem Cell Techniques Course Total Capital Funds Requested \$ 1,650 Facilities Contact Mr. Benjamin F Morris V.P., Facilities Services Facilities Services Scripps Research Institute 10550 North Torrey Pines Road | |
|--|--|
| Total Part Two Funds Requested for Stem Cell Techniques Course Total Capital Funds Requested \$ 1,650 Facilities Contact Mr. Benjamin F Morris V.P., Facilities Services Facilities Services Scripps Research Institute | |
| Total Capital Funds Requested \$ 1,650 Facilities Contact Mr. Benjamin F Morris V.P., Facilities Services Facilities Services Scripps Research Institute | |
| Facilities Contact Mr. Benjamin F Morris V.P., Facilities Services Facilities Services Scripps Research Institute | |
| Mr. Benjamin F Morris V.P., Facilities Services Facilities Services Scripps Research Institute | |
| V.P., Facilities Services Facilities Services Scripps Research Institute | |
| TPC-16 La Jolla, CA 92037 (858) 784-8088 bmorris@scripps.edu | |
| Authorized Organizational Official Date | |
| Print Name Title | |
| Program Director Date | |
| Print Name Title (Payised 03/07/2007) | |



| Project Informat | ion | | |
|-----------------------|-----------------------------|------------------------|--|
| Application Number | CL1-00502-1 | Program Director Name: | |
| Historical Perfor | | | |
| Provide information o | n past performance for 3 pr | ojects. | |

| | Project 1 | Project 2 | Project 3 |
|--------------------------------------|------------------------|-----------|-----------|
| | SR202-208 Modification | | |
| | | | |
| Brief Project Title | | | |
| Original Budget (Total project cost) | \$ 154,697 | | |
| Final project cost | \$ 156,932 | | |
| Scheduled Completion Date | Jan 15, 2007 | | |
| Actual Notice of Completion Date | Feb 15, 2007 | | |
| Gross Square Feet involved | 11,000 | | |
| Assignable Square Feet involved | 8,500 | | |
| Approximate number of change orders | 7 | | |
| Value of all change orders & claims | \$ 17,000 | | |
| Type of construction management | In-house Forces | | |

Laboratory Alteration Projects Please enter the number of laboratory alteration projects completed by the applicant in the past 2 years (in the range of \$1-5 million in project cost), and the approximate total dollar value that these projects represent. Total Laboratory Alteration Projects 1 Approximate Total Value \$ 156,932



TSRI
FACILITIES PLANNING
&
CONSTRUCTION

3030 SCIENCE PARK - LAB 3020

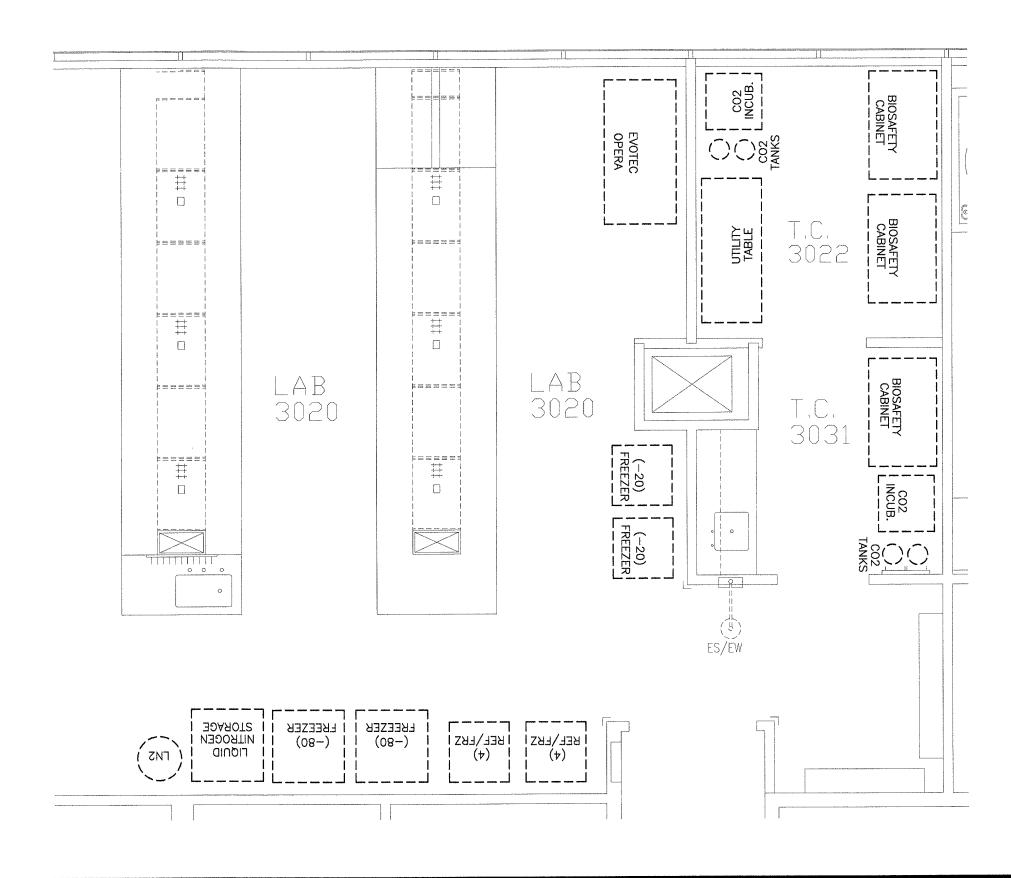
DRAWING:

FLOOR PLAN

SCALE: 1/4" = 1'-0"

OT DATE:

LOT DATE: 3-13-07



TSRI
FACILITIES PLANNING &

**
**TRUCTIO*

DRAWING: EQUIPMENT PLAN

3030 SCIENCE PARK - LAB 3020

SCALE: 1/4" = 1'-0"

PLOT DATE: 3-13-07



Application: CL1-00502-1

Title: TSRI Center for hESC Research

Public Abstract:

The therapeutic use of stem cells in regenerative medicine will require the ability to control stem cell expansion and differentiation into specific tissue types, such as pancreatic β-cells, heart tissue, bone or specific neuronal lineages. We have taken a chemical approach toward this problem in which large collections of synthetic small molecules are being screened in cell-based assays to identify drug-like molecules that control stem cell processes. Preliminary experiments in our institute have demonstrated that we can identify molecules that control the self-renewal and directed differentiation of murine embryonic stem cells. The characterization of the biological mechanisms of the molecules has also provided new insights into the underlying biology of stem cells. We now propose to extend these studies to hESC lines not eligible for federal funding, for which our research activities have been restricted to date. In addition, such lines may be better suited for specific applications, including the use of small molecules to derive specific cell lineages and investigate ES derived cell-based models of genetic disease. To this end, we would like to establish a human embryonic stem cell core facility. This facility will house the necessary equipment to genetically manipulate and culture hESCs on a large scale for a variety of studies including cell-based screens of small molecule libraries, as well as screens of arrayed genomic cDNA and siRNA libraries. We anticipate that this facility will serve our faculty as well as other labs that would like to collaboratively exploit this chemical approach to the study and manipulation of stem cells.

Statement of Benefit to California:

Historically, small molecules have been more useful than genetic approaches in the treatment of human disease. However, much of our ability to control embryonic stem cell self-renewal and directed differentiation currently involves genetic manipulation of these cells or complex mixtures of protein factors. The demonstration that one can systematically identify, optimize and characterize the mechanism of action of small drug-like molecules that selectively control stem cell biology both in vitro and in vivo will: (1) provide important tools to manipulate stem cells in the lab; (2) provide new insights into the complex biology that regulates stem cell differentiation; and (3) provide an important first step which may ultimately lead to drugs that facilitate the clinical application of stem cells.